tory, both in Garching, Germany, announce that they have picked up x-rays from a very young brown dwarf. The x-rays are probably produced in the outermost layers of the brown dwarf, as a result of strong magnetic activity. The finding suggests that the brown dwarf is rotating very rapidly; otherwise there would be no strong dynamo effect to generate the magnetic field.

Above the restless surface of a brown dwarf, astronomers expected to find an equally changeable atmosphere. The heat of a normal star would break up most compounds, but the relatively low temperatures around a brown dwarf, below 1500 kelvin, allow many more compounds to form and condense into solid particles. "We expect a very rich cloud physics in brown dwarfs," says Burrows. According to Jonathan Lunine of the University of Arizona's Lunar and Planetary Laboratory, the clouds could consist of heat-resistant silicates, plus a host of trace compounds, including ones containing sulfur and chlorine. "The chemistry can be complex," says Lunine. Burrows calls it "a fascinating mess."

Tinney and Tolley caught a glimpse of this mess using a novel instrument on the 3.9-meter Anglo-Australian Telescope to look for clouds of titanium oxide, chosen because it absorbs light strongly as a gas. The instrument, called the Taurus Tuneable Filter, enabled them to make accurate brightness measurements of a brown dwarf in two very narrow wavelength bands, one of which coincides with the absorption wavelength of gaseous titanium oxide. If clouds of titanium-bearing condensates were forming in the atmosphere of the brown dwarf, the depletion of gaseous titanium oxide would increase the brightness in this wavelength band relative to the other.

A faint brown dwarf called DENIS-PJ1228-157 did not show the effect, but observations of the much brighter brown dwarf LP 944-20, made in February and August, both revealed telltale variations of a few percent in the ratio of the two brightnesses, sometimes over just a few hours. The observations say nothing about the actual cloud structure, such as the thickness or extent of the clouds or whether they are scattered randomly or in equatorial bands as in the atmosphere of Jupiter. But Tinney and Tolley calculate, from the brightness variations they observed, that if clouds covered 5% of the visible disk of the star, the cloud tops would appear 400 degrees cooler than the surface of the star.

Burrows cautions that the researchers' conclusions are not yet conclusive. But he says that as observers continue to cast a weather eye on brown dwarfs, "we should soon know whether this exciting variability is real." **–GOVERT SCHILLING**

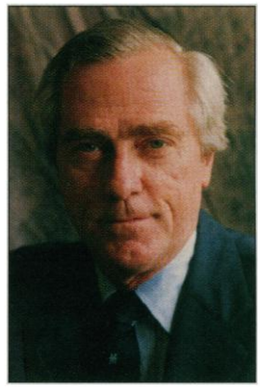
Govert Schilling is an astronomy writer in Utrecht, the Netherlands.

GENETIC DISEASES

# RAC Confronts in Utero Gene Therapy Proposals

A National Institutes of Health (NIH) advisory committee last week began what could be a long debate over whether to permit the next step in gene therapy: correcting genetic defects in a fetus before birth. Researchers say they may be ready to attempt such an experiment in 2 or 3 years, but fetal gene therapy carries potential new risks and ethical implications—including the possibility that transplanted genes could end up in sperm or egg (germ) cells and be passed on to future generations.

NIH's Recombinant DNA Advisory Committee (RAC) began to confront those issues at a 2-day meeting on 24 and 25 September when it discussed two "preprotocols" for in utero therapies submitted by W. French Anderson, a geneticist at the University of Southern California in Los Angeles. Anderson was part of an NIH team that performed the first gene therapy experiments on humans 8 years ago. Although Anderson says he needs to do more animal studies before he draws up a solid protocol, he submitted his preliminary proposals to the RAC to force discussion of the risks early on. "It is imperative to do everything possible" to reduce the chance of germ line gene transfer, says Anderson.



**Fetal therapy.** W. French Anderson catalyzes a debate.

Anderson is hoping to test in utero gene therapy on two potentially fatal diseases: homozygous α-thalassemia, a hemoglobin disorder so severe that it kills the fetus before birth, and a severe immunodeficiency caused by lack of the enzyme adenosine deaminase (ADA). The protocol for treating α-thalassemia involves mixing fetal blood with a retroviral vector carrying a functioning copy of the gene missing or defective in α-thalassemia, which makes the protein α globin, and then transfusing the treated blood back into the fetus. The hope is that the virus will insert the gene into stem cells—the blood cell precursors—which are more prevalent in fetal than adult blood. This procedure might only partially correct the defect, in which case the child could be born with developmental abnormalities, or with transfusion-dependent thalassemia. But because the genetic manipulations would be performed outside the womb, it would pose little risk of the gene entering the fetus's germ line.

The likelihood of that happening would be much greater, however, with Anderson's proposal for correcting ADA deficiency. The preprotocol calls for injecting a retroviral vector carrying the ADA gene directly into the fetus's peritoneal cavity. Based on studies in sheep, he expects the vector to carry the gene into the rapidly dividing stem cells of the bone marrow, which produce the cells of the immune system. But the vector could also find its way into germ line cells.

That prospect raised concerns among the 15 regular RAC members and the eight ad hoc participants invited to review the preprotocols. "This is a lightning-rod issue," says LeRoy Walters, director of the Kennedy Institute of Ethics at Georgetown University in Washington, D.C., and an ad hoc reviewer. The big worry is that the transferred gene could cause deleterious mutations that could be passed to future generations. "Nobody knows quite what's going to happen," says RAC Chair Claudia Mickelson of the Massachusetts Institute of Technology.

Anderson acknowledged that the risk of germ line transfer can't be eliminated. But he expects it to be very low—one in a million sperm might be affected, he guesses—and it could have positive effects or none at all. Most committee members seemed convinced. Evelyn Karson, an ad hoc reviewer and director of the Division of Reproductive Genetics at Washington, D.C.'s, Columbia Hospital for Women, noted that relatively few people would receive fetal therapy, and the number of mutations would be far outpaced by those occurring naturally. "Our genes just get picked up and tossed like a big tossed salad every time we undergo reproduction," she says.

For now, committee members called for more experiments to assess both the risks of the proposed protocols and their chance of success. As even Anderson concedes, "we do not have data to answer" whether in utero gene therapy will succeed. "There's a whole lot of work that needs to be done," says committee member Philip Noguchi, director of the Division of Cellular and Gene Therapies at the Food and Drug Administration.

The committee proposed that long-term studies on in utero gene transfer in sheep and many generations of mice be conducted to supplement the thin and somewhat ambiguous animal data that now exist. It also suggested that different diseases be considered as candidates, such as other immune deficiencies that are even harder to treat than ADA-deficiency. Until those experiments are done, RAC members say they are keeping an open mind about in utero gene therapy. **–JENNIFER COUZIN**